THE COLLOIDAL GOLD TEST IN CEREBRO SPINAL FLUIDS

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THE object of this article is to state our experiences and conclusions with the title subject. While further work leading out of this study has been interrupted, it has seemed advisable to give such results as we have obtained.

The published work upon this test is for the most part favourable, but the earlier hopes that it would serve to detect different types of syphilis of the central nervous system and different types of meningitis are not being realized.

In the following table is summarized the results of the examination of one hundred and eight specimens of spinal fluid. The cases are grouped according to the clinical diagnosis. No other tests have been made to parallel the colloidal gold test throughout the series, but the Wassermann test has been made in over 60 per cent. of the cases and has been noted. In the tabulation of our results we have expressed the curve of colour change after the manner of Lee and Hinton[2] thus: No change=0; slight change=1; red blue=2; violet=3; blue water=4; water clear (complete precipitation)=5. In this way the result appears as a series of ten numbers representing the degree of colour change in the ten tubes of the test, beginning with the 1:10 dilution and ending with the 1:5120 dilution. In the larger groups of cases to avoid listing a long series of numbers, we have determined roughly what might be termed an average and a mode formula, the former representing the approximate average change of colour in each tube, and the latter the series of colour changes to which the majority of the cases conform.

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Clinical Diagnosis	No. of Cases	Wassermann Test			Reading of Individual Cases	Average Reading of Group	Mode	Remarks
		Pos.	Neg.	Unknown				
General Paresis.....	25	20	..	5	.....	4445444321	5555554320	
Cerebro-spinal Syphilis.....	2	1	..	..	0112332100	.....	.....	
		1	..	..	0045555555	.....	.....	No autopsies.
Epilepsy.....	43	0	25	..	.....	1111111111	0111000000	
		..	..	18	.....	1111000000	0000000000	
Meningitis.....		..	1	..	0000000444	.....	.....	(Streptococcus mucosus)
		..	..	1	0000012343	.....	.....	B. tuberculosis.
		..	..	1	0000000345	.....	.....	Streptococcus.
		..	..	1	0001113443	.....	.....	Pneumococcus.
		..	..	1	0000002554	.....	.....	Meningococcus.
		..	..	1	0000000442	.....	.....	"
		..	..	1	0000003331	.....	.....	"
		..	..	1	0000000455	.....	.....	"
		..	..	1	0000244211	.....	.....	"
		..	..	1	0000033542	.....	.....	
All forms.....	10	..	..	..	.....	0000012443	0000000444	
Meningismus.....	3	..	..	..	.....	0000000000	0000000000	

Clinical Diagnosis	No. of Cases	Wassermann Test			Reading of Individual Cases	Average Reading of Group	Mode	Remarks
		Pos.	Neg.	Unknown				
Brain tumour.....	3	..	..	1	0000000000	.....	.....	No autopsy.
		..	1	..	0001100000	.....	.....	No autopsy.
		..	1	..	0014421000	.....	.....	Endothelioma.
Huntingdon's Chorea	2	..	..	1	1233220000	.....	.....	
		..	1	..	2234300000	.....	.....	
Manic, Depressive.....	5	..	..	1	0000000000	.....	.....	
		..	..	1	0000000000	.....	.....	
		..	1	..	0000000000	.....	.....	
		..	..	1	0000000000	.....	.....	
		..	..	1	1221100000	.....	.....	
Dementia Præcox.....	5	..	..	1	0000000000	.....	.....	
		..	1	..	0021110000	.....	.....	
		..	1	..	0000000000	.....	.....	
		1	..	..	1100000000	.....	.....	Under treatment.
		..	1	..	0000000000	.....	.....	
Unknown.....	10	..	10	..	.....	0111100000	0001100000	

The cases of general paresis were typical with the exception of one in which the clinical course suggested a possible dementia præcox plus a syphilitic infection. The spinal fluid, however, showed increased cells, increase of globulin, a typical curve with colloidal gold, and a strongly positive Wassermann. The curve for paresis was quite uniform in all cases except two in which the depth of colour change reached only to the point three. This occurred in the fourth tube in the one case and the fourth and fifth in the other.

The two cases diagnosed clinically as cerebro-spinal syphilis did not come to autopsy. The curves are distinctly different. From our experience with other fluids we do not believe that a curve for cerebro-spinal syphilis exists which can be distinguished from curves obtained with some non-syphilitic conditions, as for instance the case of endothelioma of the brain.

In five cases of epilepsy change of colour to the point three occurred. In two cases change of colour reached four, and in two others five. In all of these the Wassermann was negative. The curves may perhaps be accounted for by some admixture of blood serum, for further investigation of epileptics showed their spinal fluids to be practically inactive and they failed to give any characteristic curve. Also we have concluded in agreement with Swalm and Mann[6] that slight grades of colour change are not significant.

The curve in two cases of Huntingdon's chorea is interesting in being approximately the same, but no conclusions can be drawn.

Of the cases diagnosed as brain tumour only one came to autopsy and this was a case in which a suggestion of gumma was made from the colloidal gold test and the occurrence of a doubtful Wassermann in the blood serum. Later, however, a negative Wassermann was obtained in blood and spinal fluid and the post-mortem examination showed a large endothelioma.

The group of cases of meningitis is interesting as showing agreement in the position of maximum colour change in the end zone in spite of a variety of infective agents. There is even more agreement here than in the group of five cases of tuberculous meningitis mentioned by Grulee and Moody.[4] It should be pointed out that in any form of acute meningitis with the location of the bacterial irritant upon the brain coverings, there will be added to the normal cerebro-spinal fluid in varying quantities the elements of an inflammatory exudate which in its fluid part will consist largely of the constituents of blood serum.

We have found that if spinal fluids which show no change with

colloidal gold have added to them varying proportions of blood serum before the test is set up, such mixtures will give reactions which are practically identical with those obtained in suppurative or tuberculous meningitis. When one tenth or more serum is present the height of colour change usually occurs in the last four dilutions of the series. Decreasing the proportion of serum tends to cause the maximum point of colour change to travel towards the left so that curves occur in the mid zone though the degree of change may not be as great.

This suggests that quantitative differences in the exudate in the spinal canal will produce different curves with colloidal gold and may offer some explanation of Grulee and Moody's findings. It also demonstrates the importance of having fluids uncontaminated by even minute quantities of blood serum, and also casts some doubt on the value of midzonal curves. It is doubtful too, if end zone precipitation should be accounted of any value in the diagnosis of meningitis if unaccompanied by an increase of cells.

In the group marked "meningismus?" one case was typhoid fever, but the other two may have been abortive types of epidemic meningitis for there was an increase of cells but no definite increase of globulin and the patients recovered, one without any further puncturing and the other after receiving a dose of antimeningitis serum at the time of the first puncture, and only one other puncture thereafter.

A group of cases is listed where the clinical diagnosis was not obtained but in which the Wassermann reactions were negative. No precipitation occurred in the luetic zone with any of these cases. The constancy of the curve in general paresis has suggested that the substance responsible for the precipitation of the colloidal gold may be the same as that constituent of blood and spinal fluid which accounts for a positive Wassermann reaction. Recently, however, Weston[8] has concluded that the substances concerned are not identical.

Repetition of the experiments with mixtures of blood serum and spinal fluid and repeated tests on the same fluid with different indicators has disclosed the fact that there is sometimes a distinct variation in the sensitiveness of the colloidal gold solutions even when made by the same method. We also tried solutions made by the use of a small crystal of pyrogallic acid in place of the formaldehyde solution. These indicators although of a beautiful ruby colour were sometimes such comparatively stable colloids

as to be unaffected by the fluid of a typical paretic or by salt solutions of considerable strength.

Colloidal solutions are said to vary according to the electrification, size and number of their particles. In the case of the gold solution the electrification does not alter in quality but certainly by different methods of preparation it can be shown that the number and size of the particle will vary to such a degree that some solutions will precipitate where others will remain quite inactive with the same and even larger quantities of protein or electrolyte. That variations occur in the precipitability of colloidal gold solutions made by the formaldehyde method we believe to be not infrequent, and hence differences in curves with fluids from the same type of case may result not from quantitative differences in the fluids but from qualitative differences in the indicators. It is quite evident that in the Lange test the preparation of the gold solution by the formaldehyde method must be adhered to, but it may be advisable to test every indicator for its sensitiveness either by the use of a known paretic fluid or possibly by titration with an electrolyte. We have endeavoured to arrive at a colloidal gold solution of definite sensitiveness by setting up a series of ten tubes containing chemically normal NaCl from ·05 c.c. to .5 c.c. making up to constant volume and then adding 5 c.c. of indicator. It would seem to us unwise to use an indicator which will not precipitate in at least the last five tubes of such a series.

Our conclusions concerning this test at the present stage of our experience with it we may summarize thus:

1. The colloidal gold test in cerebro-spinal fluid forms a valuable confirmatory test for general paresis.

2. No constant curve of precipitation occurs in epilepsy.

3. A very small admixture of blood serum will render results unreliable.

4. No special significance can be attached to curves with the maximum of precipitation in the mid zone.

5. Slight degrees of colour change are not significant.

6. Maximum precipitation in the end zone occurs in most cases of acute meningitis but there is no definite relation to the causative organism.

7. Each indicator should be tested for its sentitiveness before use.

References:

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The Miramichi Hospital at Newcastle, New Brunswick, was formally opened on July 1st. The hospital is the gift of Mr. Ernest Hutchison. The building is of native sandstone and overlooks the Miramichi River; it has a frontage of 144 feet, with an average depth of 40 feet, and is equipped with every modern convenience including an *x*-ray room, an electric elevator, and laundry. The cost of maintenance will be borne by public subscription and endowments amounting to about $6,000 have already been made. Accommodation is provided for from forty to fifty patients.